DEPARTMENT OF HEALTH AND HUMAN SERVICES

NOTE TO FILE

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Keywords:

Corn, *Zea mays*, Herbicide Resistance, Glyphosate (N-phosphonomethyl-glycine), 5-enolypyruvylshikimate-3-phosphate synthase (EPSPS)

Background

In a submission dated August 19,1997, Monsanto provided summary information to support their safety assessment of genetically modified corn (Zea mays), specifically transformation event GA21 and progeny derived therefrom. As a supporting document, this submission also contained the safety and nutritional assessment of Roundup Ready corn line GA21.

Intended Effect and Food/Feed Use

The intended technical effect of this genetic modification of corn is to confer tolerance to the herbicidal compound N-phosphonomethyl-glycine, the active moiety of glyphosate (Roundup).

According to Monsanto, their Roundup Ready corn line GA21 has been modified to express a modified version of the corn enzyme 5-enolypyruvylshikimate-3-phosphate synthase (EPSPS). The modified version of EPSPS has been reported to be tolerant to glyphosate.

Molecular Alterations and Characterization

Monsanto described the partial identity and function of the genetic material introduced into corn by a particle acceleration transformation system using agarose gel-isolated plasmid vector fragments. The modified EPSPS gene was transformed into corn after being insolated on a fragment of the plasmid vector pDPG434. The fragment contained only the modified corn EPSPS gene fused to an optimized chloroplast transit peptide sequence, under control of the rice actin promoter and intron, and a nontranslated region of the nopaline synthase (NOS) gene from *Agrobacterium* in the form of a gene cassette. The exact construction details of the plasmid pDPG434 are considered by Monsanto to be confidential business information.

Monsanto presented data and information that allowed the firm to conclude that corn line GA21 contains one DNA insert. The insert contains two copies of the modified corn EPSPS gene cassette, and a third copy which has been demonstrated to contain the rice actin promoter and modified EPSPS gene without the NOS end. The insert did not contain any DNA from outside the modified corn EPSPS gene cassette, the DNA intended to be transferred. Monsanto also presented evidence that the insert remained stably

integrated in the plant genome through six successive generations and was inherited in accordance to the Mendelian single gene model.

Expressed Protein

One new protein, the modified enzyme 5-enolypyruvylshikimate-3-phosphate synthase (EPSPS), is expressed in the corn line GA21. Monsanto stated that the EPSPS enzyme confers the glyphosate-tolerant phenotype because the modified EPSPS has a reduced affinity for glyphosate. EPSPS enzymes have a common function and are found in all plants.

Monsanto presented data and information that allowed the firm to conclude that 1) the modified EPSPS protein is not known to be an allergen; 2) the modified EPSPS does not bear sequence homology to known allergens and toxins; 3) the modified EPSPS protein shows a high (99.3%) sequence homology to the wild type corn enzyme as well as to other EPSPSs found in food crops; 4) the modified EPSPS protein is rapidly degraded under simulated gastric conditions; and 5) dietary exposure to the modified EPSPS protein will be very low.

Compositional Analysis

Monsanto presented data that allowed the firm to conclude that the Roundup Ready corn line GA21 is not materially different in any meaningful way from corn varieties now being sold except for the tolerance to Roundup herbicide. Monsanto presented the results of extensive compositional analyses that demonstrate that the levels of important components in corn grain (protein, fat, carbohydrate, ash, acid detergent and neutral detergent fiber, fatty acids, amino acids, and moisture) and forage (protein, fat, carbohydrate, ash, acid detergent and neutral detergent fiber, calcium, phosphorus and moisture) in this line are comparable to nontransgenic corn control lines and to available published literature ranges.

Conclusions

Monsanto has concluded that corn containing transformation event GA21 is not materially different in composition, nutrition, and safety from corn currently grown, processed, marketed, and consumed for animal feed or human food. At this time, based on Monsanto's description of its data and analyses, the Agency considers Monsanto's consultation on corn from varieties containing transformation event GA21 to be complete.

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